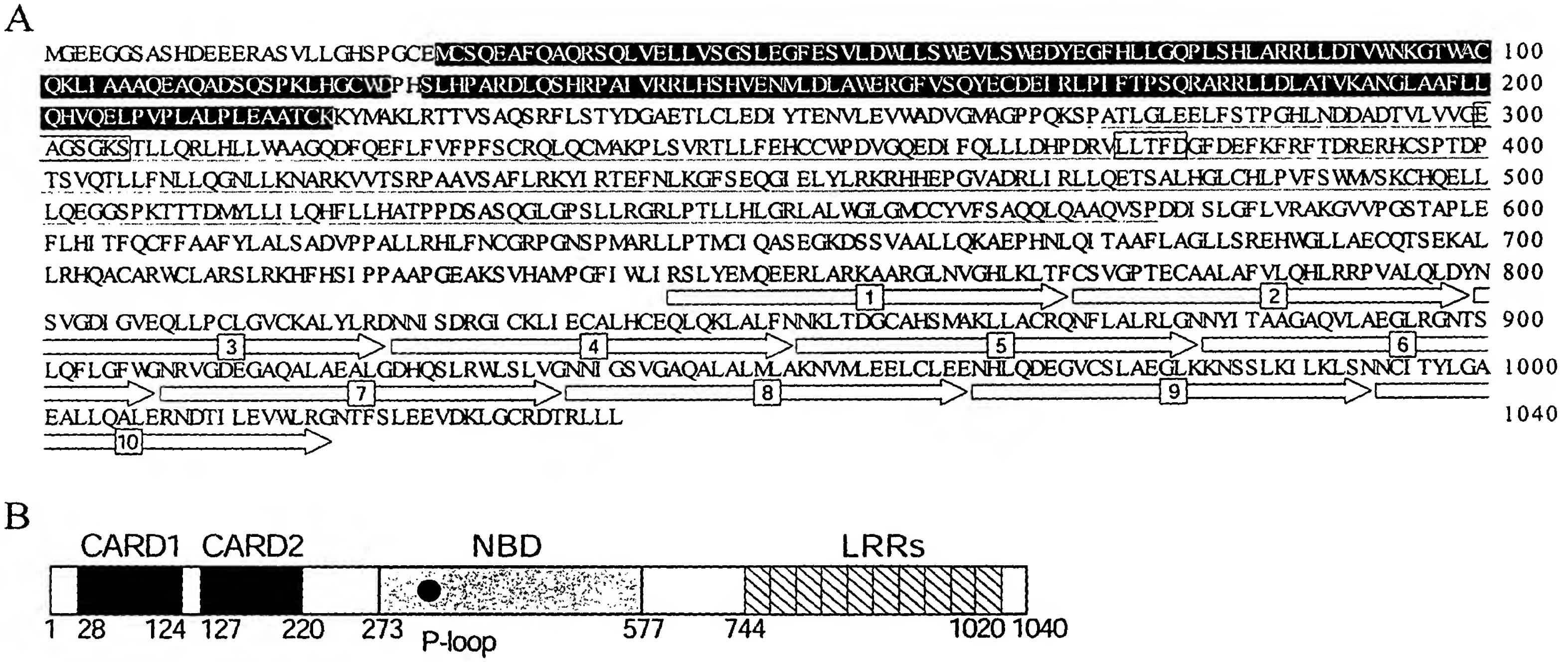

A
MGEEGGSASHDEEERASVLLGHSPGCEMCSQEAFQAQRSQLVELLVSGSLEGFESVLDWLLSWEVLSWEDYEGFHLLGQPLSHLARRLLDTVWNKGTWAC 100
QKLIAAAQEAQADSQSPKLHGCWDPHSLHPARDLQSHRPAIVRRLHSHVENMLDLAWERGFVSQYECDEIRLPIFTPSQRARRLLDLATVKANGLAAFLL 200
QHVQELPVPLALPLEAATCKKYMAKLRTTVSAQSRFLSTYDGAETLCLEDIYTENVLEVWADVGMAGPPQKSPATLGLEELFSTPGHLNDDADTVLVVGE 300
AGSGKSTLLQRLHLLWAAGQDFQEFLFVFPFSCRQLQCMAKPLSVRTLLFEHCCWPDVGQEDIFQLLLDHPDRVLLTFDGFDEFKFRFTDRERHCSPTDP 400
TSVQTLLFNLLQGNLLKNARKVVTSRPAAVSAFLRKYIRTEFNLKGFSEQGIELYLRKRHHEPGVADRLIRLLQETSALHGLCHLPVFSWMVSKCHQELL 500
LQEGGSPKTTTDMYLLILQHFLLHATPPDSASQGLGPSLLRGRLPTLLHLGRLALWGLGMCCYVFSAQQLQAAQVSPDDISLGFLVRAKGVVPGSTAPLE 600
FLHITFQCFFAAFYLALSADVPPALLRHLFNCGRPGNSPMARLLPTMCIQASEGKDSSVAALLQKAEPHNLQITAAFLAGLLSREHWGLLAECQTSEKAL 700
LRHQACARWCLARSLRKHFHSIPPAAPGEAKSVHAMPGFIWLIRSLYEMQEERLARKAARGLNVGHLKLTFCSVGPTECAALAFVLQHLRRPVALQLDYN 800
1
2
SVGDIGVEQLLPCLGVCKALYLRDNNISDRGICKLIECALHCEQLQKLALFNNKLTDGCAHSMAKLLACRQNFLALRLGNNYITAAGAQVLAEGLRGNTS 900
3
4
5
6
LQFLGFWGNRVGDEGAQALAEALGDHQSLRWLSLVGNNIGSVGAQALALMLAKNVMLEELCLEENHLQDEGVCSLAEGLKKNSSLKILKLSNNCITYLGA 1000
7
8
9
EALLQALERNDTILEVWLRGNTFSLEEVDKLGCRDTRLLL 1040
10
B
CARD1
CARD2
NBD
LRRs
1
28
124
127
220
273
P-loop
577
744
1020
1040

Figure 1

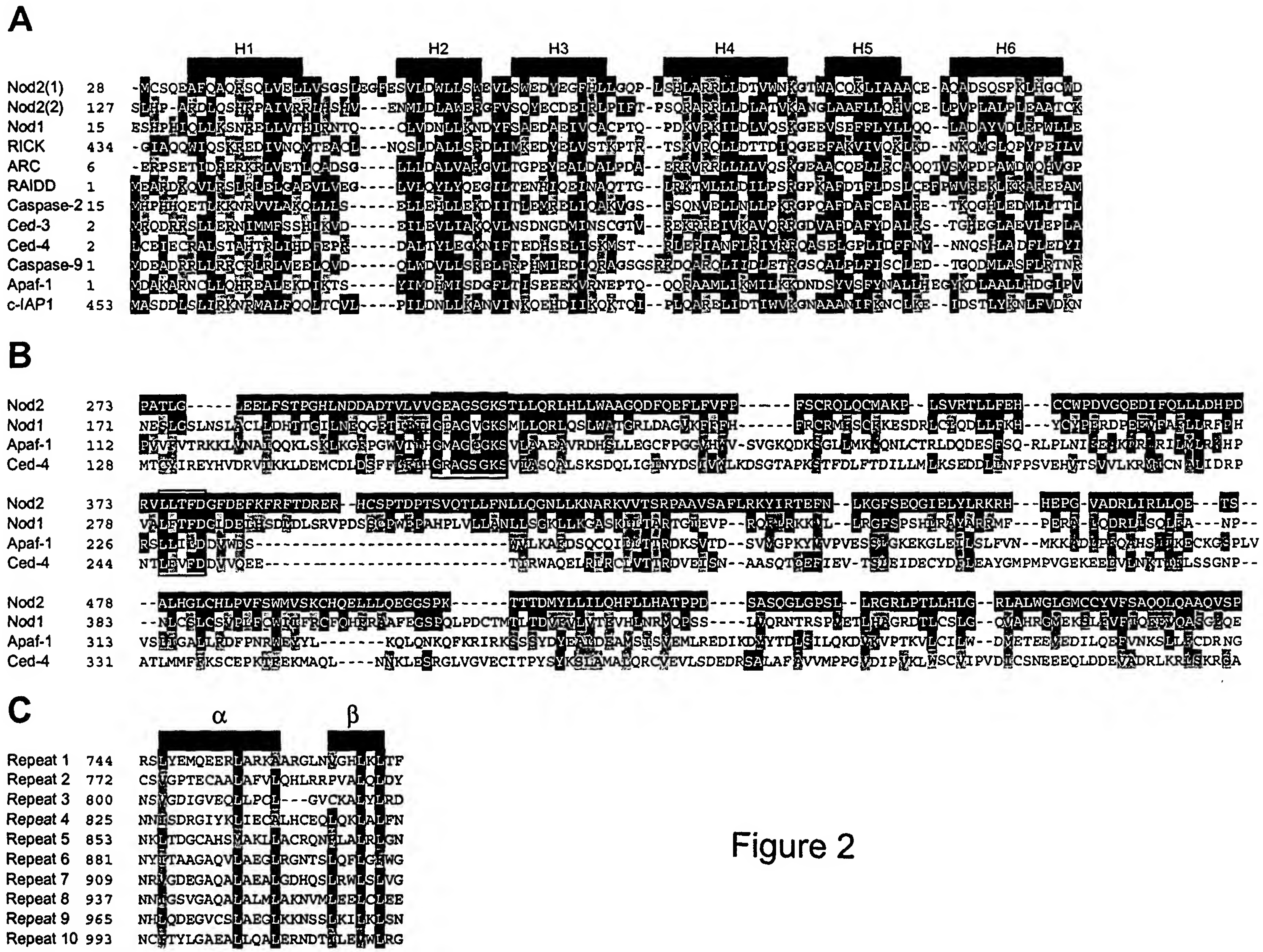
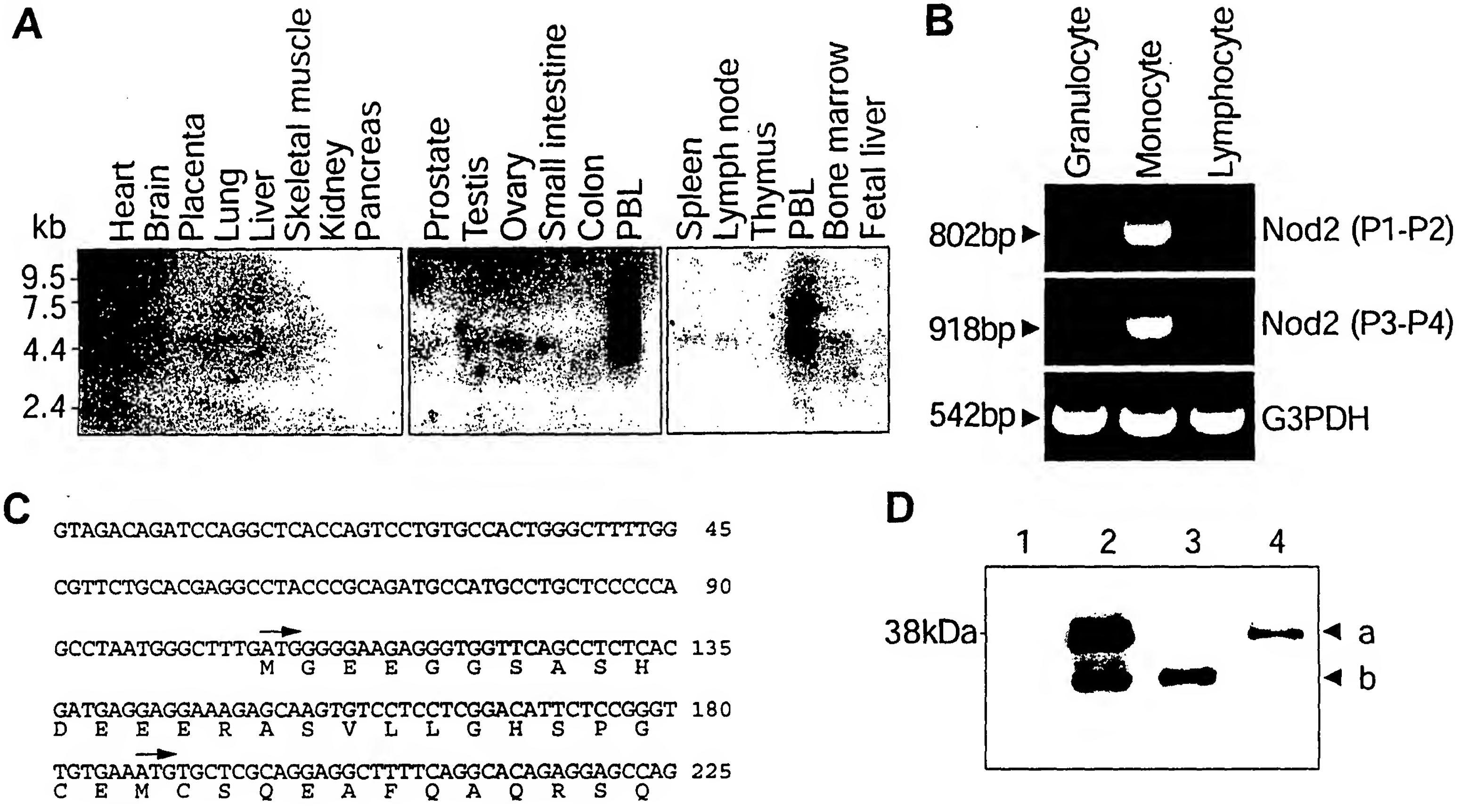

A
H1
H2
H3
H4
H5
H6
Nod2(1) 28
Nod2(2) 127
Nod1 15
RICK 434
ARC 6
RAIDD 1
Caspase-2 15
Ced-3 2
Ced-4 2
Caspase-9 1
Apaf-1 1
c-IAP1 453
B
Nod2 273
Nod1 171
Apaf-1 112
Ced-4 128
Nod2 373
Nod1 278
Apaf-1 226
Ced-4 244
Nod2 478
Nod1 383
Apaf-1 313
Ced-4 331
C
α
β
Repeat 1 744
Repeat 2 772
Repeat 3 800
Repeat 4 825
Repeat 5 853
Repeat 6 881
Repeat 7 909
Repeat 8 937
Repeat 9 965
Repeat 10 993

Figure 2



```
GTAGACAGATCCAGGCTCACCAGTCCTGTGCCACTGGGCTTTTGG  45

CGTTCTGCACGAGGCCTACCCGCAGATGCCATGCCTGCTCCCCCA  90

GCCTAATGGGCTTTGATGGGGGAAGAGGGTGGTTCAGCCTCTCAC 135
               M  G  E  E  G  G  S  A  S  H
GATGAGGAGGAAAGAGCAAGTGTCCTCCTCGGACATTCTCCGGGT 180
D  E  E  E  R  A  S  V  L  L  G  H  S  P  G
TGTGAAATGTGCTCGCAGGAGGCTTTTCAGGCACAGAGGAGCCAG 225
C  E  M  C  S  Q  E  A  F  Q  A  Q  R  S  Q
```

Figure 3

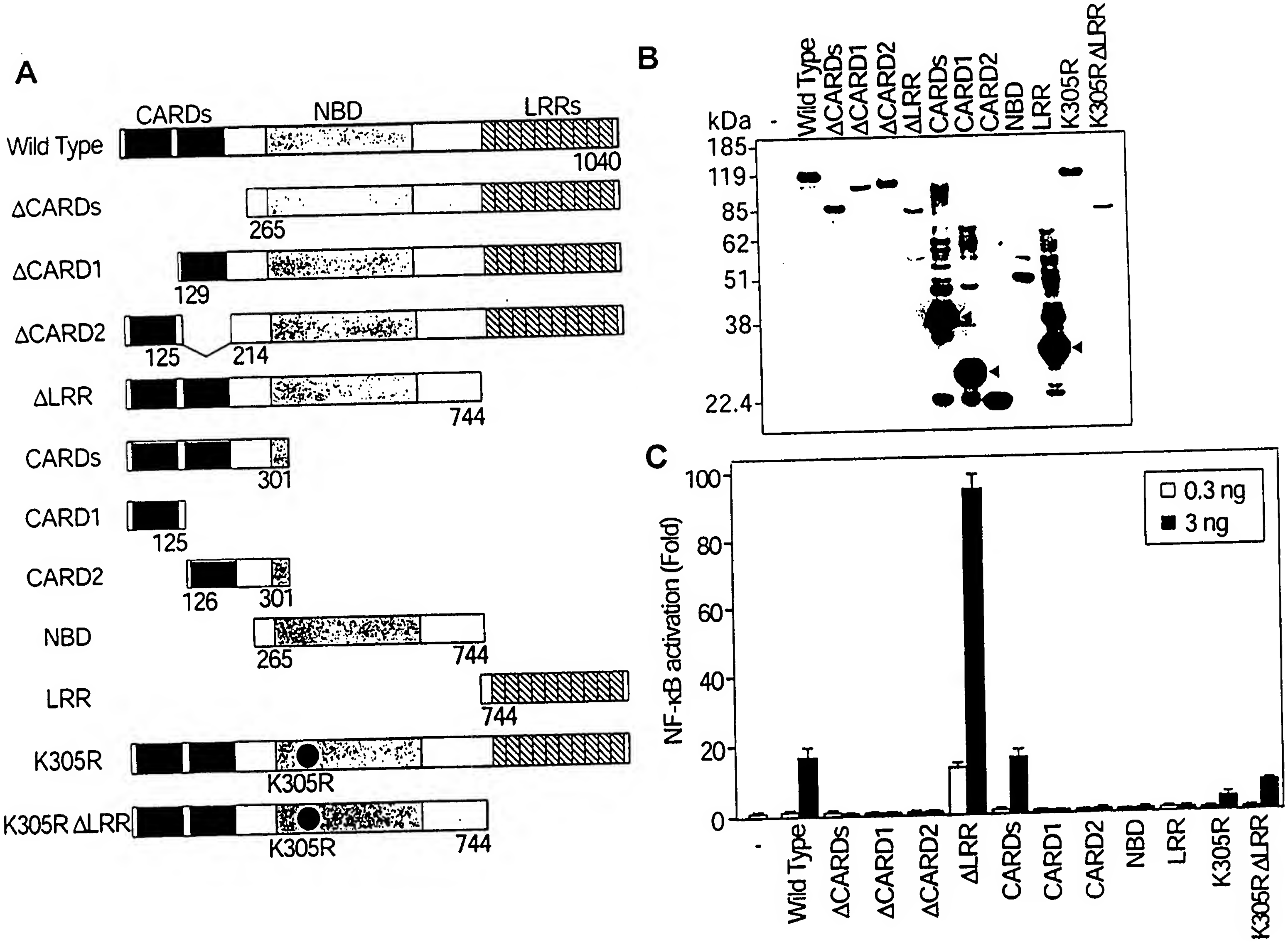

A
CARDs
NBD
LRRs
Wild Type
1040
ΔCARDs
265
ΔCARD1
129
ΔCARD2
125
214
ΔLRR
744
CARDs
301
CARD1
125
CARD2
126
301
NBD
265
744
LRR
744
K305R
K305R
K305R ΔLRR
K305R
744
B
kDa
-
Wild Type
ΔCARDs
ΔCARD1
ΔCARD2
ΔLRR
CARDs
CARD1
CARD2
NBD
LRR
K305R
K305R ΔLRR
185
119
85
62
51
38
22.4
C
NF-κB activation (Fold)
100
80
60
40
20
0
□ 0.3 ng
■ 3 ng
-
Wild Type
ΔCARDs
ΔCARD1
ΔCARD2
ΔLRR
CARDs
CARD1
CARD2
NBD
LRR
K305R
K305R ΔLRR

Figure 4

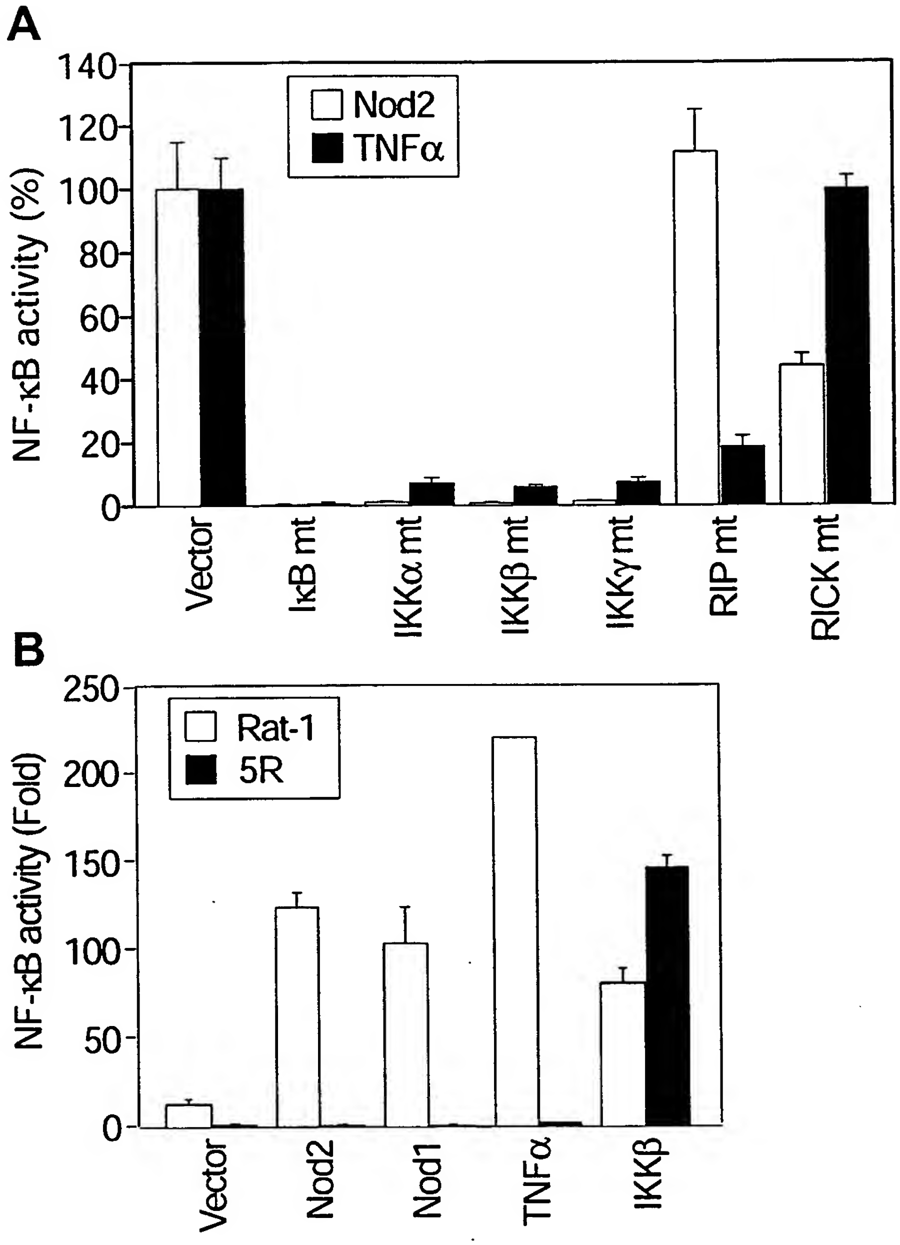

A
NF-κB activity (%)
140
120
100
80
60
40
20
0
□ Nod2
■ TNFα
Vector
IκB mt
IKKα mt
IKKβ mt
IKKγ mt
RIP mt
RICK mt
B
NF-κB activity (Fold)
250
200
150
100
50
0
□ Rat-1
■ 5R
Vector
Nod2
Nod1
TNFα
IKKβ

Figure 5

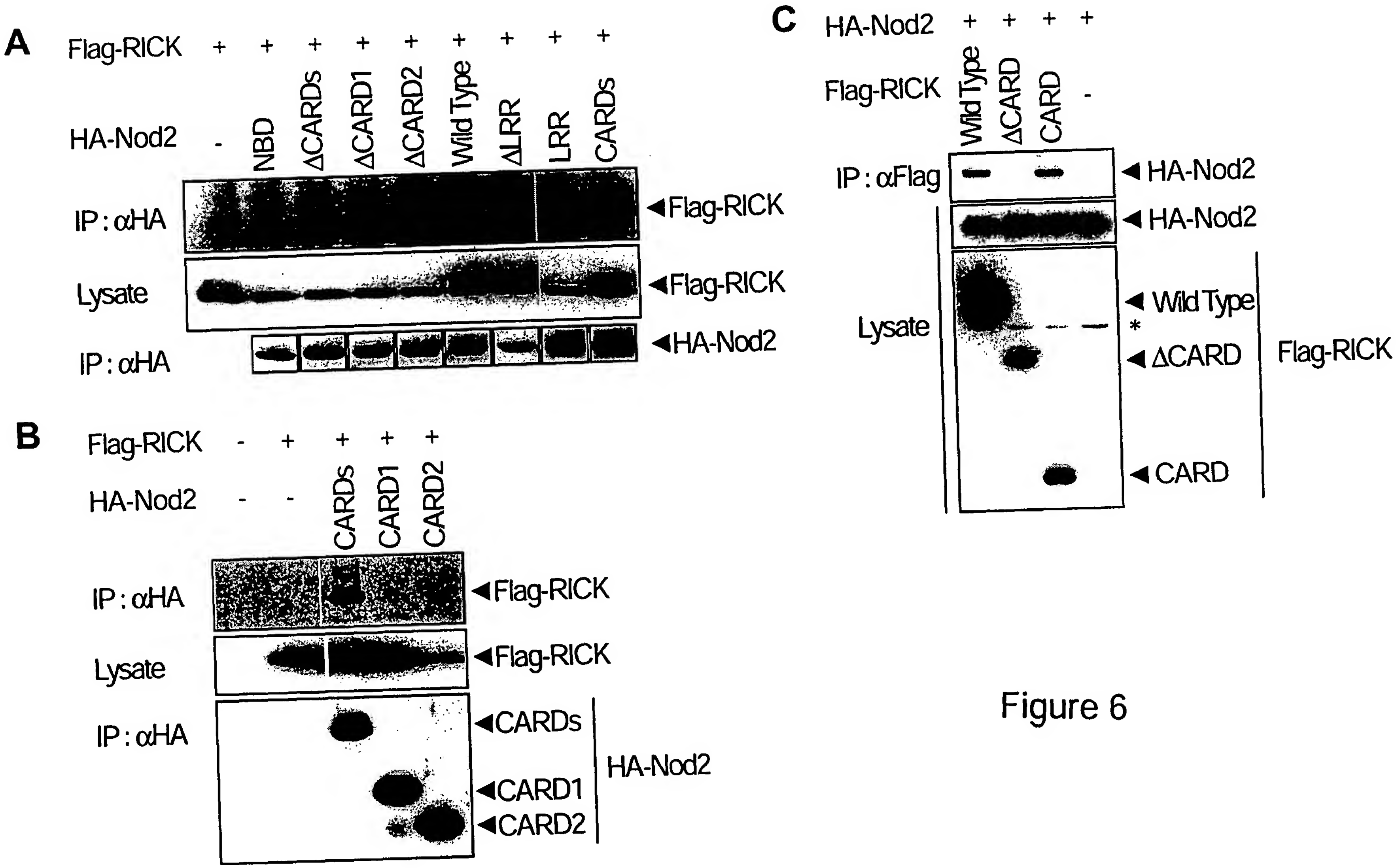

A
Flag-RICK + + + + + + + + +
HA-Nod2 - NBD ΔCARDs ΔCARD1 ΔCARD2 Wild Type ΔLRR LRR CARDs
IP : αHA
◀Flag-RICK
Lysate
◀Flag-RICK
IP : αHA
◀HA-Nod2
B
Flag-RICK - + + + +
HA-Nod2 - - CARDs CARD1 CARD2
IP : αHA
◀Flag-RICK
Lysate
◀Flag-RICK
IP : αHA
◀CARDs
◀CARD1
◀CARD2
HA-Nod2
C
HA-Nod2 + + + +
Flag-RICK Wild Type ΔCARD CARD -
IP : αFlag
◀HA-Nod2
◀HA-Nod2
Lysate
◀ Wild Type
*
◀ΔCARD
◀CARD
Flag-RICK

Figure 6

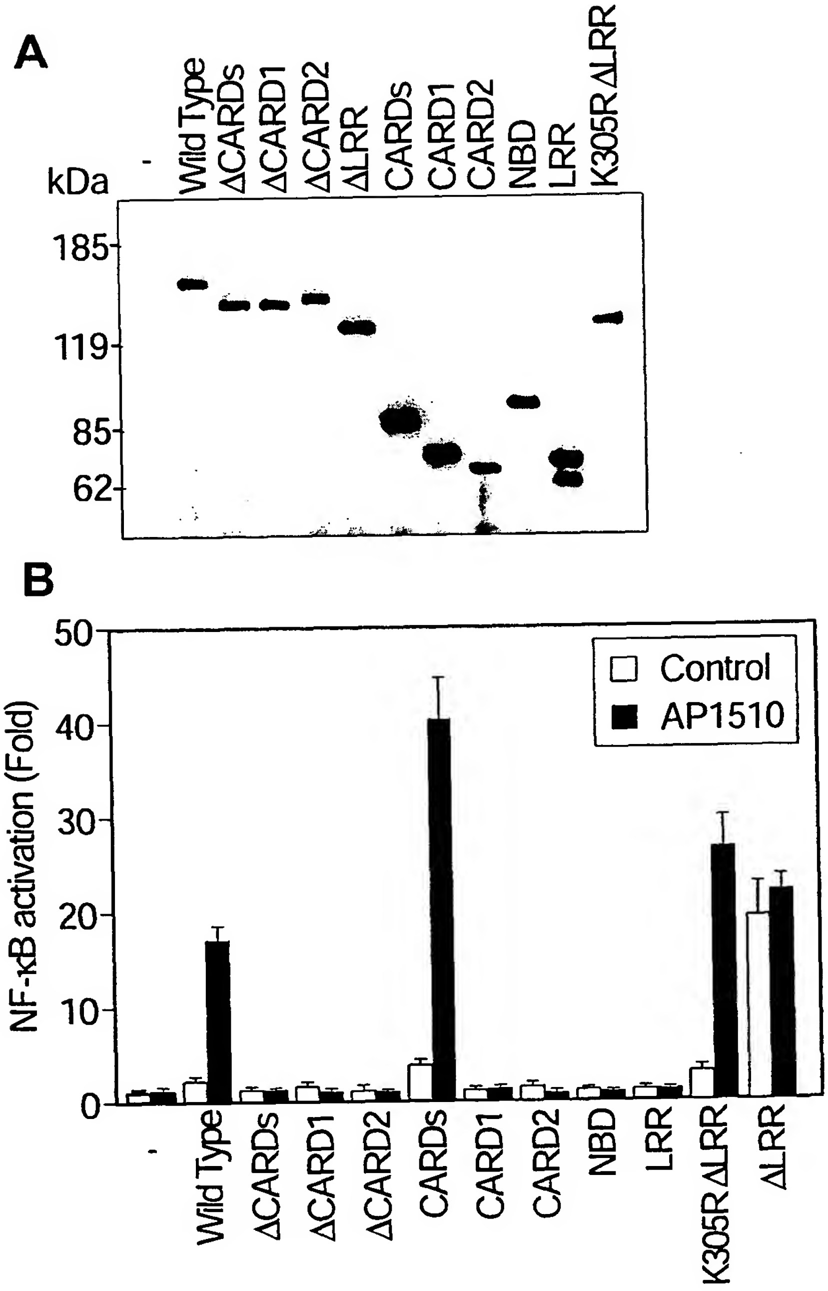

A
kDa
-
Wild Type
ΔCARDs
ΔCARD1
ΔCARD2
ΔLRR
CARDs
CARD1
CARD2
NBD
LRR
K305R ΔLRR
185
119
85
62
B
NF-κB activation (Fold)
50
40
30
20
10
0
☐ Control
■ AP1510
-
Wild Type
ΔCARDs
ΔCARD1
ΔCARD2
CARDs
CARD1
CARD2
NBD
LRR
K305R ΔLRR
ΔLRR

Figure 7

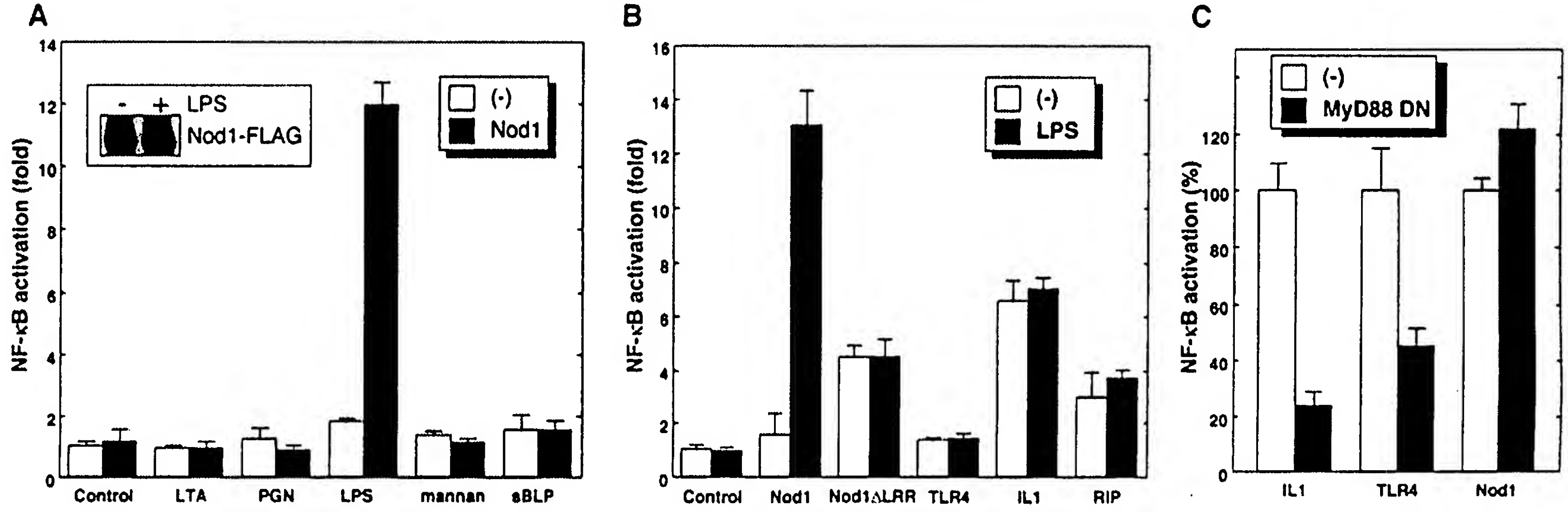

A
NF-κB activation (fold)
0
2
4
6
8
10
12
14
- + LPS
Nod1-FLAG
□ (-)
■ Nod1
Control
LTA
PGN
LPS
mannan
sBLP
B
NF-κB activation (fold)
0
2
4
6
8
10
12
14
16
□ (-)
■ LPS
Control
Nod1
Nod1ΔLRR
TLR4
IL1
RIP
C
NF-κB activation (%)
0
20
40
60
80
100
120
□ (-)
■ MyD88 DN
IL1
TLR4
Nod1

Figure 8

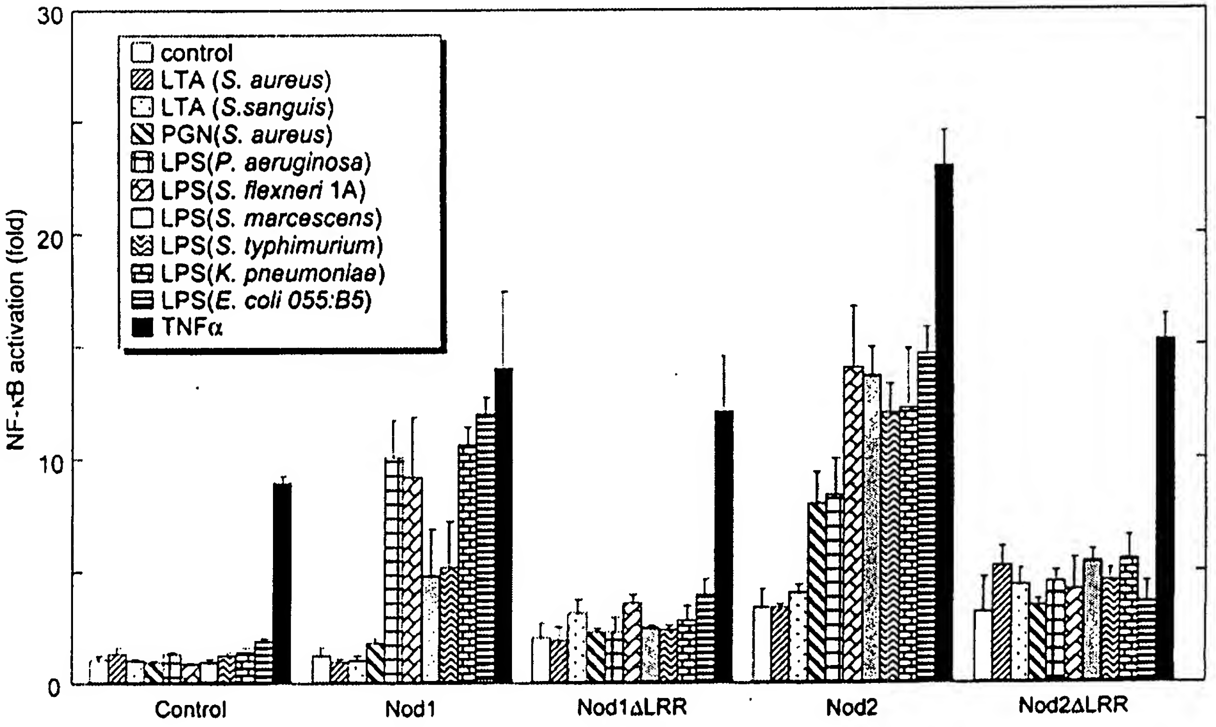

NF-κB activation (fold)
0
10
20
30
□ control
▨ LTA (*S. aureus*)
▨ LTA (*S.sanguis*)
▨ PGN(*S. aureus*)
▨ LPS(*P. aeruginosa*)
▨ LPS(*S. flexneri* 1A)
□ LPS(*S. marcescens*)
▨ LPS(*S. typhimurium*)
▨ LPS(*K. pneumoniae*)
▤ LPS(*E. coli 055:B5*)
■ TNFα
Control
Nod1
Nod1ΔLRR
Nod2
Nod2ΔLRR

Figure 9

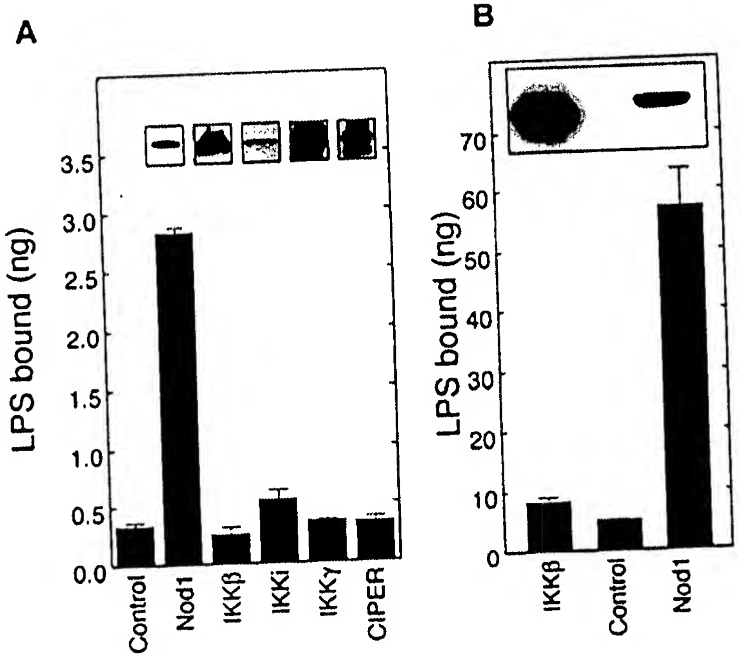

A
LPS bound (ng)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
Control
Nod1
IKKβ
IKKi
IKKγ
CIPER
B
LPS bound (ng)
0
10
20
30
40
50
60
70
IKKβ
Control
Nod1

Figure 10

# Figure 11

# SEQ ID NO:33

Nod2 cDNA sequence

```
gtagacagat ccaggctcac cagtcctgtg ccactgggct tttggcgttc tgcacaaggc     60
ctacccgcag atgccatgcc tgctccccca gcctaatggg ctttgatggg ggaagagggt    120
ggttcagcct ctcacgatga ggaggaaaga gcaagtgtcc tcctcggaca ttctccgggt    180
tgtgaaatgt gctcgcagga ggcttttcag gcacagagga gccagctggt cgagctgctg    240
gtctcagggt ccctggaagg cttcgagagt gtcctggact ggctgctgtc ctgggaggtc    300
ctctcctggg aggactacga gggcttccac ctcctgggcc agcctctctc ccacttggcc    360
aggcgccttc tggacaccgt ctggaataag ggtacttggg cctgtcagaa gctcatcgcg    420
gctgcccaag aagcccaggc cgacagccag tcccccaagc tgcatggctg ctgggacccc    480
cactcgctcc acccagcccg agacctgcag agtcaccggc cagccattgt caggaggctc    540
cacagccatg tggagaacat gctggacctg gcatgggagc ggggtttcgt cagccagtat    600
gaatgtgatg aaatcaggtt gccgatcttc acaccgtccc agagggcaag aaggctgctt    660
gatcttgcca cggtgaaagc gaatggattg gctgccttcc ttctacaaca tgttcaggaa    720
ttaccagtcc cattggccct gcctttggaa gctgccacat gcaagaagta tatggccaag    780
ctgaggacca cggtgtctgc tcagtctcgc ttcctcagta cctatgatgg agcagagacg    840
ctctgcctgg aggacatata cacagagaat gtcctggagg tctgggcaga tgtgggcatg    900
gctggacccc cgcagaagag cccagccacc ctgggcctgg aggagctctt cagcacccct    960
ggccacctca atgacgatgc ggacactgtg ctggtggtgg gtgaggcggg cagtggcaag   1020
agcacgctcc tgcagcggct gcacttgctg tgggctgcag ggcaagactt ccaggaattt   1080
ctctttgtct tcccattcag ctgccggcag ctgcagtgca tggccaaacc actctctgtg   1140
cggactctac tctttgagca ctgctgttgg cctgatgttg gtcaagaaga catcttccag   1200
ttactccttg accaccctga ccgtgtcctg ttaacctttg atggctttga cgagttcaag   1260
ttcaggttca cggatcgtga acgccactgc tccccgaccg accccacctc tgtccagacc   1320
```

ctgctcttca accttctgca gggcaacctg ctgaagaatg cccgcaaggt ggtgaccagc 1380

cgtccggccg ctgtgtcggc gttcctcagg aagtacatcc gcaccgagtt caacctcaag 1440

ggcttctctg aacagggcat cgagctgtac ctgaggaagc gccatcatga gcccggggtg 1500

gcggaccgcc tcatccgcct gctccaagag acctcagccc tgcacggttt gtgccacctg 1560

cctgtcttct catggatggt gtccaaatgc caccaggaac tgttgctgca ggaggggggg 1620

tccccaaaga ccactacaga tatgtacctg ctgattctgc agcattttct gctgcatgcc 1680

acccccccag actcagcttc ccaaggtctg ggacccagtc ttcttcgggg ccgcctcccc 1740

accctcctgc acctgggcag actggctctg tggggcctgg gcatgtgctg ctacgtgttc 1800

tcagcccagc agctccaggc agcacaggtc agccctgatg acatttctct tggcttcctg 1860

gtgcgtgcca aaggtgtcgt gccagggagt acggcgcccc tggaattcct tcacatcact 1920

ttccagtgct tctttgccgc gttctacctg gcactcagtg ctgatgtgcc accagctttg 1980

ctcagacacc tcttcaattg tggcaggcca ggcaactcac caatggccag gctcctgccc 2040

acgatgtgca tccaggcctc ggagggaaag gacagcagcg tggcagcttt gctgcagaag 2100

gccgagccgc acaaccttca gatcacagca gccttcctgg cagggctgtt gtcccgggag 2160

cactggggcc tgctggctga gtgccagaca tctgagaagg ccctgctccg gcgccaggcc 2220

tgtgcccgct ggtgtctggc ccgcagcctc cgcaagcact tccactccat cccgccagct 2280

gcaccgggtg aggccaagag cgtgcatgcc atgcccgggt tcatctggct catccggagc 2340

ctgtacgaga tgcaggagga gcggctggct cggaaggctg cacgtggcct gaatgttggg 2400

cacctcaagt tgacattttg cagtgtgggc cccactgagt gtgctgccct ggcctttgtg 2460

ctgcagcacc tccggcggcc cgtggccctg cagctggact acaactctgt gggtgacatt 2520

ggcgtggagc agctgctgcc ttgccttggt gtctgcaagg ctctgtattt gcgcgataac 2580

aatatctcag accgaggcat ctgcaagctc attgaatgtg ctcttcactg cgagcaattg 2640

cagaagttag ctctattcaa caacaaattg actgacggct gtgcacactc catggctaag 2700

ctccttgcat gcaggcagaa cttcttggca ttgaggctgg ggaataacta catcactgcc 2760

gcgggagccc aagtgctggc cgaggggctc cgaggcaaca cctccttgca gttcctggga 2820

ttctggggca acagagtggg tgacgagggg gcccaggccc tggctgaagc cttgggtgat 2880

caccagagct tgaggtggct cagcctggtg gggaacaaca ttggcagtgt gggtgcccaa 2940

gccttggcac tgatgctggc aaagaacgtc atgctagaag aactctgcct ggaggagaac 3000

catctccagg atgaaggtgt atgttctctc gcagaaggac tgaagaaaaa ttcaagtttg 3060

aaaatcctga agttgtccaa taactgcatc acctacctag ggcagaagcc cctcctgcag 3120

gccccttgaaa ggaatgacac catcctggaa gtctggctcc gagggaacac tttctctcta 3180

gaggaggttg acaagctcgg ctgcagggac accagactct tgctttgaag tctccgggag 3240

gatgttcgtc tcagtttgtt tgtgagcagg ctgtgagttt gggccccaga ggctgggtga 3300

catgtgttgg cagcctcttc aaaatgagcc ctgtcctgcc taaggctgaa cttgttttct 3360

gggaacacca taggtcacct ttattctggc agaggaggga gcatcagtgc cctccaggat 3420

agacttttcc caagcctact tttgccattg acttcttccc aagattcaat cccaggatgt 3480

acaaggacag cccctcctcc atagtatggg actggcctct gctgatcctc ccaggcttcc 3540

gtgtgggtca gtggggccca tggatgtgct tgttaactga gtgccttttg gtggagaggc 3600

ccggcctctc acaaaagacc ccttaccact gctctgatga agaggagtac acagaacaca 3660

taattcagga agcagctttc cccatgtctc gactcatcca tccaggccat tccccgtctc 3720

tggttcctcc cctcctcctg gactcctgca cacgctcctt cctctgaggc tgaaattcag 3780

aatattagtg acctcagctt tgatatttca cttacagcac cccccaaccct ggcacccagg 3840

gtgggaaggg ctacacctta gcctgccctc ctttccggtg tttaagacat ttttggaagg 3900

ggacacgtga cagccgtttg ttccccaaga cattctaggt ttgcaagaaa aatatgacca 3960

cactccagct gggatcacat gtggactttt atttccagtg aaatcagtta ctcttcagtt 4020

aagcctttgg aaacagctcg actttaaaaa gctccaaatg cagctttaaa aaattaatct 4080

gggccagaat ttcaaacggc ctcactaggc ttctggttga tgcctgtgaa ctgaactctg 4140

acaacagact tctgaaatag acccacaaga ggcagttcca tttcatttgt gccagaatgc 4200

tttaggatgt acagttatgg attgaaagtt tacaggaaaa aaaattaggc cgttccttca 4260

aagcaaatgt cttcctggat tattcaaaat gatgtatgtt gaagcctttg taaattgtca 4320

gatgctgtgc aaatgttatt attttaaaca ttatgatgtg tgaaaactgg ttaatattta 4380

taggtcactt tgttttactg tcttaagttt atactcttat agacaacatg gccgtgaact 4440

ttatgctgta aataatcaga ggggaataaa ctgttgagtc aaaac 4485

# Figure 12

# SEQ ID NO:1

Nod2 cDNA sequence

```
gtagacagat ccaggctcac cagtcctgtg ccactgggct tttggcgttc tgcacaaggc        60
ctacccgcag atgccatgcc tgctccccca gcctaatggg ctttgatggg ggaagagggt       120
ggttcagcct ctcacgatga ggaggaaaga gcaagtgtcc tcctcggaca ttctccgggt       180
tgtgaaatgt gctcgcagga ggcttttcag gcacagagga gccagctggt cgagctgctg       240
gtctcagggt ccctggaagg cttcgagagt gtcctggact ggctgctgtc ctgggaggtc       300
ctctcctggg aggactacga gggcttccac ctcctgggcc agcctctctc ccacttggcc       360
aggcgccttc tggacaccgt ctggaataag ggtacttggg cctgtcagaa gctcatcgcg       420
gctgcccaag aagcccaggc cgacagccag tcccccaagc tgcatggctg ctgggacccc       480
cactcgctcc acccagcccg agacctgcag agtcaccggc cagccattgt caggaggctc       540
cacagccatg tggagaacat gctggacctg gcatgggagc ggggtttcgt cagccagtat       600
gaatgtgatg aaatcaggtt gccgatcttc acaccgtccc agagggcaag aaggctgctt       660
gatcttgcca cggtgaaagc gaatggattg gctgccttcc ttctacaaca tgttcaggaa       720
ttaccagtcc cattggccct gcctttggaa gctgccacat gcaagaagta tatggccaag       780
ctgaggacca cggtgtctgc tcagtctcgc ttcctcagta cctatgatgg agcagagacg       840
ctctgcctgg aggacatata cacagagaat gtcctggagg tctgggcaga tgtgggcatg       900
gctggacccc cgcagaagag cccagccacc ctgggcctgg aggagctctt cagcacccct       960
ggccacctca atgacgatgc ggacactgtg ctggtggtgg gtgaggcggg cagtggcaag      1020
agcacgctcc tgcagcggct gcacttgctg tgggctgcag ggcaagactt ccaggaattt      1080
ctctttgtct tcccattcag ctgccggcag ctgcagtgca tggccaaacc actctctgtg      1140
cggactctac tctttgagca ctgctgttgg cctgatgttg gtcaagaaga catcttccag      1200
ttactccttg accaccctga ccgtgtcctg ttaacctttg atggctttga cgagttcaag      1260
ttcaggttca cggatcgtga acgccactgc tccccgaccg accccacctc tgtccagacc      1320
```

```
ctgctcttca accttctgca gggcaacctg ctgaagaatg cccgcaaggt ggtgaccagc     1380
cgtccggccg ctgtgtcggc gttcctcagg aagtacatcc gcaccgagtt caacctcaag     1440
ggcttctctg aacagggcat cgagctgtac ctgaggaagc gccatcatga gcccggggtg     1500
gcggaccgcc tcatccgcct gctccaagag acctcagccc tgcacggttt gtgccacctg     1560
cctgtcttct catggatggt gtccaaatgc caccaggaac tgttgctgca ggaggggggg     1620
tccccaaaga ccactacaga tatgtacctg ctgattctgc agcatttttct gctgcatgcc    1680
accccccccag actcagcttc ccaaggtctg ggacccagtc ttcttcgggg ccgcctcccc    1740
accctcctgc acctgggcag actggctctg tggggcctgg gcatgtgctg ctacgtgttc     1800
tcagcccagc agctccaggc agcacaggtc agccctgatg acatttctct tggcttcctg     1860
gtgcgtgcca aaggtgtcgt gccagggagt acggcgcccc tggaattcct tcacatcact     1920
ttccagtgct tctttgccgc gttctacctg gcactcagtg ctgatgtgcc accagctttg     1980
ctcagacacc tcttcaattg tggcaggcca ggcaactcac caatggccag gctcctgccc     2040
acgatgtgca tccaggcctc ggagggaaag gacagcagcg tggcagcttt gctgcagaag     2100
gccgagccgc acaaccttca gatcacagca gccttcctgg cagggctgtt gtcccgggag     2160
cactggggcc tgctggctga gtgccagaca tctgagaagg ccctgctccg gcgccaggcc     2220
tgtgcccgct ggtgtctggc ccgcagcctc cgcaagcact tccactccat cccgccagct     2280
gcaccgggtg aggccaagag cgtgcatgcc atgcccgggt tcatctggct catccggagc     2340
ctgtacgaga tgcaggagga gcggctggct cggaaggctg cacgtggcct gaatgttggg     2400
cacctcaagt tgacattttg cagtgtgggc cccactgagt gtgctgccct ggcctttgtg     2460
ctgcagcacc tccggcggcc cgtggccctg cagctggact acaactctgt gggtgacatt     2520
ggcgtggagc agctgctgcc ttgccttggt gtctgcaagg ctctgtattt gcgcgataac     2580
aatatctcag accgaggcat ctgcaagctc attgaatgtg ctcttcactg cgagcaattg     2640
cagaagttag ctctattcaa caacaaattg actgacggct gtgcacactc catggctaag     2700
ctccttgcat gcaggcagaa cttcttggca ttgaggctgg ggaataacta catcactgcc     2760
gcgggagccc aagtgctggc cgaggggctc cgaggcaaca cctccttgca gttcctggga     2820
ttctggggca acagagtggg tgacgagggg gcccaggccc tggctgaagc cttgggtgat     2880
caccagagct tgaggtggct cagcctggtg gggaacaaca ttggcagtgt gggtgcccaa     2940
gccttggcac tgatgctggc aaagaacgtc atgctagaag aactctgcct ggaggagaac     3000
catctccagg atgaaggtgt atgttctctc gcagaaggac tgaagaaaaa ttcaagtttg     3060
aaaatcctga agttgtccaa taactgcatc acctacctag ggcagaagcc ctcctgcag      3120
```

gcccttgaaa ggaatgacac catcctggaa gtctggctcc gagggaacac tttctctcta 3180

gaggaggttg acaagctcgg ctgcagggac accagactct tgctttgaag tctccgggag 3240

gatgttcgtc tcagtttgtt tgtgagcagg ctgtgagttt gggccccaga ggctgggtga 3300

catgtgttgg cagcctcttc aaaatgagcc ctgtcctgcc taaggctgaa cttgttttct 3360

gggaacacca taggtcacct ttattctggc agaggaggga gcatcagtgc cctccaggat 3420

agacttttcc caagcctact tttgccattg acttcttccc aagattcaat cccaggatgt 3480

acaaggacag cccctcctcc atagtatggg actggcctct gctgatcctc ccaggcttcc 3540

gtgtgggtca gtggggccca tggatgtgct tgttaactga gtgccttttg gtggagaggc 3600

ccggcctctc acaaaagacc ccttaccact gctctgatga agaggagtac acagaacaca 3660

taattcagga agcagctttc cccatgtctc gactcatcca tccaggccat tccccgtctc 3720

tggttcctcc cctcctcctg gactcctgca cacgctcctt cctctgaggc tgaaattcag 3780

aatattagtg acctcagctt tgatatttca cttacagcac ccccaaccct ggcacccagg 3840

gtgggaaggg ctacacctta gcctgccctc ctttccggtg tttaagacat ttttggaagg 3900

ggacacgtga cagccgtttg ttccccaaga cattctaggt ttgcaagaaa aatatgacca 3960

cactccagct gggatcacat gtggactttt atttccagtg aaatcagtta ctcttcagtt 4020

aagcctttgg aaacagctcg actttaaaaa gctccaaatg cagctttaaa aaattaatct 4080

gggccagaat ttcaaacggc ctcactaggc ttctggttga tgcctgtgaa ctgaactctg 4140

acaacagact tctgaaatag acccacaaga ggcagttcca tttcatttgt gccagaatgc 4200

tttaggatgt acagttatgg attgaaagtt tacaggaaaa aaaattaggc cgttccttca 4260

aagcaaatgt cttcctggat tattcaaaat gatgtatgtt gaagcctttg taaattgtca 4320

gatgctgtgc aaatgttatt attttaaaca ttatgatgtg tgaaaactgg ttaatattta 4380

taggtcactt tgttttactg tcttaagttt atactcttat agacaacatg gccgtgaact 4440

ttatgctgta aataatcaga ggggaataaa ctgttgagtc aaaac 4485

# Figure 13

## SEQ ID NO:2

MGEEGGSASH DEEERASVLL GHSPGCEMCS QEAFQAQRSQ LVELLVSGSL EGFESVLDWL
LSWEVLSWED YEGFHLLGQP LSHLARRLLD TVWNKGTWAC QKLIAAAQEA QADSQSPKLH
GCWDPHSLHP ARDLQSHRPA IVRRLHSHVE NMLDLAWERG FVSQYECDEI RLPIFTPSQR
ARRLLDLATV KANGLAAFLL QHVQELPVPL ALPLEAATCK KYMAKLRTTV SAQSRFLSTY
DGAETLCLED IYTENVLEVW ADVGMAGPPQ KSPATLGLEE LFSTPGHLND DADTVLVVGE
AGSGKSTLLQ RLHLLWAAGQ DFQEFLFVFP FSCRQLQCMA KPLSVRTLLF EHCCWPDVGQ
EDIFQLLLDH PDRVLLTFDG FDEFKFRFTD RERHCSPTDP TSVQTLLFNL LQGNLLKNAR
KVVTSRPAAV SAFLRKYIRT EFNLKGFSEQ GIELYLRKRH HEPGVADRLI RLLQETSALH
GLCHLPVFSW MVSKCHQELL LQEGGSPKTT TDMYLLILQH FLLHATPPDS ASQGLGPSLL
RGRLPTLLHL GRLALWGLGM CCYVFSAQQL QAAQVSPDDI SLGFLVRAKG VVPGSTAPLE
FLHITFQCFF AAFYLALSAD VPPALLRHLF NCGRPGNSPM ARLLPTMCIQ ASEGKDSSVA
ALLQKAEPHN LQITAAFLAG LLSREHWGLL AECQTSEKAL LRRQACARWC LARSLRKHFH
SIPPAAPGEA KSVHAMPGFI WLIRSLYEMQ EERLARKAAR GLNVGHLKLT FCSVGPTECA
ALAFVLQHLR RPVALQLDYN SVGDIGVEQL LPCLGVCKAL YLRDNNISDR GICKLIECAL
HCEQLQKLAL FNNKLTDGCA HSMAKLLACR QNFLALRLGN NYITAAGAQV LAEGLRGNTS
LQFLGFWGNR VGDEGAQALA EALGDHQSLR WLSLVGNNIG SVGAQALALM LAKNVMLEEL
CLEENHLQDE GVCSLAEGLK KNSSLKILKL SNNCITYLGA EALLQALERN DTILEVWLRG
NTFSLEEVDK LGCRDTRLLL *

# Figure 14

## SEQ ID NO:3

MCSQEAFQAQ RSQLVELLVS GSLEGFESVL DWLLSWEVLS WEDYEGFHLL GQPLSHLARR
LLDTVWNKGT WACQKLIAAA QEAQADSQSP KLHGCWDPHS LHPARDLQSH RPAIVRRLHS
HVENMLDLAW ERGFVSQYEC DEIRLPIFTP SQRARRLLDL ATVKANGLAA FLLQHVQELP
VPLALPLEAA TCKKYMAKLR TTVSAQSRFL STYDGAETLC LEDIYTENVL EVWADVGMAG
PPQKSPATLG LEELFSTPGH LNDDADTVLV VGEAGSGKST LLQRLHLLWA AGQDFQEFLF
VFPFSCRQLQ CMAKPLSVRT LLFEHCCWPD VGQEDIFQLL LDHPDRVLLT FDGFDEFKFR
FTDRERHCSP TDPTSVQTLL FNLLQGNLLK NARKVVTSRP AAVSAFLRKY IRTEFNLKGF
SEQGIELYLR KRHHEPGVAD RLIRLLQETS ALHGLCHLPV FSWMVSKCHQ ELLLQEGGSP
KTTTDMYLLI LQHFLLHATP PDSASQGLGP SLLRGRLPTL LHLGRLALWG LGMCCYVFSA
QQLQAAQVSP DDISLGFLVR AKGVVPGSTA PLEFLHITFQ CFFAAFYLAL SADVPPALLR
HLFNCGRPGN SPMARLLPTM CIQASEGKDS SVAALLQKAE PHNLQITAAF LAGLLSREHW
GLLAECQTSE KALLRRQACA RWCLARSLRK HFHSIPPAAP GEAKSVHAMP GFIWLIRSLY
EMQEERLARK AARGLNVGHL KLTFCSVGPT ECAALAFVLQ HLRRPVALQL DYNSVGDIGV
EQLLPCLGVC KALYLRDNNI SDRGICKLIE CALHCEQLQK LALFNNKLTD GCAHSMAKLL
ACRQNFLALR LGNNYITAAG AQVLAEGLRG NTSLQFLGFW GNRVGDEGAQ ALAEALGDHQ
SLRWLSLVGN NIGSVGAQAL ALMLAKNVML EELCLEENHL QDEGVCSLAE GLKKNSSLKI
LKLSNNCITY LGAEALLQAL ERNDTILEVW LRGNTFSLEE VDKLGCRDTR LLL*

# Figure 15
## SEQ ID NO:34

Nod2a AA sequence, Mutant

```
MGEEGGSASH DEEERASVLL GHSPGCEMCS QEAFQAQRSQ LVELLVSGSL EGFESVLDWL
LSWEVLSWED YEGFHLLGQP LSHLARRLLD TVWNKGTWAC QKLIAAAQEA QADSQSPKLH
GCWDPHSLHP ARDLQSHRPA IVRRLHSHVE NMLDLAWERG FVSQYECDEI RLPIFTPSQR
ARRLLDLATV KANGLAAFLL QHVQELPVPL ALPLEAATCK KYMAKLRTTV SAQSRFLSTY
DGAETLCLED IYTENVLEVW ADVGMAGPPQ KSPATLGLEE LFSTPGHLND DADTVLVVGE
AGSGKSTLLQ RLHLLWAAGQ DFQEFLFVFP FSCRQLQCMA KPLSVRTLLF EHCCWPDVGQ
EDIFQLLLDH PDRVLLTFDG FDEFKFRFTD RERHCSPTDP TSVQTLLFNL LQGNLLKNAR
KVVTSRPAAV SAFLRKYIRT EFNLKGFSEQ GIELYLRKRH HEPGVADRLI RLLQETSALH
GLCHLPVFSW MVSKCHQELL LQEGGSPKTT TDMYLLILQH FLLHATPPDS ASQGLGPSLL
RGRLPTLLHL GRLALWGLGM CCYVFSAQQL QAAQVSPDDI SLGFLVRAKG VVPGSTAPLE
FLHITFQCFF AAFYLALSAD VPPALLRHLF NCGRPGNSPM ARLLPTMCIQ ASEGKDSSVA
ALLQKAEPHN LQITAAFLAG LLSREHWGLL AECQTSEKAL LRRQACARWC LARSLRKHFH
SIPPAAPGEA KSVHAMPGFI WLIRSLYEMQ EERLARKAAR GLNVGHLKLT FCSVGPTECA
ALAFVLQHLR RPVALQLDYN SVGDIGVEQL LPCLGVCKAL YLRDNNISDR GICKLIECAL
HCEQLQKLAL FNNKLTDGCA HSMAKLLACR QNFLALRLGN NYITAAGAQV LAEGLRGNTS
LQFLGFWGNR VGDEGAQALA EALGDHQSLR WLSLVGNNIG SVGAQALALM LAKNVMLEEL
CLEENHLQDE GVCSLAEGLK KNSSLKILKL SNNCITYLGA EALLQAP*
```

# FIGURE 16

Nod2 Exon11, Wild type

```
cagacatgag caggatgtgt ctaagggaca ggtgggcttc agtagactgg ctaactcctg

cagtctcttt aactggacag tttcaagagg aaaaccaaga atccttgaag ctcaccattg

tatcttcttt tccagGTTGT CCAATAACTG CATCACCTAC CTAGGGGCAG AAGCCCTCCT
                L  S   N  N  C   I  T  Y  L   G  A  E   A  L  L

GCAGGCCCTT GAAAGGAATG ACACCATCCT GGAAGTCTGg taaggcccct gggcaggcct
 Q  A  L   E  R  N  D   T  I  L   E  V

gttttagctc tccgaacctc agtttttcta tctgtaaaat ggggtgacgg gagagaggaa

tggcagaatt ttgaggatcc cttctgattc tgacattcag tgagaatgat tctgcatgtg
```

Nod2 Exon11, Mutant

```
cagacatgag caggatgtgt ctaagggaca ggtgggcttc agtagactgg ctaactcctg

cagtctcttt aactggacag tttcaagagg aaaaccaaga atccttgaag ctcaccattg

tatcttcttt tccagGTTGT CCAATAACTG CATCACCTAC CTAGGGGCAG AAGCCCTCCT
                L  S   N  N  C   I  T  Y  L   G  A  E   A  L  L

GCAGGCCCCT TGAAAGGAAT GACACCATCC TGGAAGTCTG gtaaggcccc tgggcaggcc
```

Q A P *

tgttttagct ctccgaacct cagtttttct atctgtaaaa tggggtgacg ggagagagga

atggcagaat tttgaggatc ccttctgatt ctgacattca gtgagaatga ttctgcatgt

g